

REMARKS

1. Status of the claims

Claims 1, 2, 4, 5, 7-9, 11, 15, 16, 18, 23, 26, 28, 30, 36, 39, 43, 44, 49, 54, 57, 59, 62, and 102 were pending in this application. Claims 3, 6, 10, 12-14, 17, 19-22, 24, 25, 27, 29, 31-35, 37, 38, 40-42, 45-48, 50-53, 55, 56, 61, 63-79, and 81-101 have been cancelled without prejudice or disclaimer. Claims 1, 4, 7-9, 11, 15, 16, 23, 26, 28, 43, 49, 57, 58, 60, 62, and 80 have been amended to clarify claim scope or to correct various informalities. New Claims 103 and 104 have been added. Support for the amendments and new claims can be found throughout the specification. For instance, amended claim 1 support can be found, for instance, in cancelled claim 52; amended claim 11 support can be found in paragraphs [0021]-[0023]; new claim 103 support can be found in paragraphs [0044] and [0045]; and new claim 104 support can be found in paragraphs [0027]-[0031] and Figure 1. Accordingly, no new matter has been added as a result of the above-described amendments. Claims 1, 2, 4, 5, 7-9, 11, 15, 16, 18, 23, 26, 28, 30, 36, 39, 43, 44, 49, 54, 57-60, 62, 80, and 102-104 are currently pending.

2. Rejection of claims 1, 2, 4, 5, 7-9, 11, 15, 16, 18, 23, 26, 28, 30, 36, 39, 43, 44, 49, 54, 57, 59, 62, and 102 under 35 U.S.C. § 102(b) in view of Delcardayre

The Office Action alleges that claims 1, 2, 4, 5, 7-9, 11, 15, 16, 18, 23, 26, 28, 30, 36, 39, 43, 44, 49, 54, 57, 59, 62, and 102 are anticipated by Delcardayre *et al.* (WO/9831837) ("Delcardayre"). The Office Action specifically states that Delcardayre discloses construction of a YAC library; concatemer expression cassettes; transformation of the YAC library into yeast cells; induction of meiosis followed by mating; and that each cell may harbor multiple YACs. Applicants respectfully disagree and traverse the rejection.

Page 5 of the Office Action states, *inter alia*, that Delcardayre does not teach or suggest an expression cassette comprising the general formula [rs2-SP-PR-X-TR-SP-rs1]_n wherein rs2 and rs1 together denote a functional restriction site, SP individually denotes a spacer of at least two nucleotide bases, PR denotes a promoter capable of functioning in a cell, X denotes an expressible nucleotide sequence, TR denotes a terminator, and n≥2. These features are recited in instant

amended claim 1. In view of the admission in the Office Action, Applicants submit that Delcardayre does not anticipate the instant claims. Applicants submit that the claims are in compliance with 35 U.S.C. § 102(b) and respectfully request that the rejection be withdrawn.

3. Rejection of claims 52, 56, 58, and 60 under 35 U.S.C. § 103(a) based on Delcardayre in view of Goldsmith

The Office Action alleges that claims 52, 56, 58, and 60 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Delcardayre, in view of Goldsmith *et al.* (WO 02/059296) (“Goldsmith”). The basis for the rejection can be found on pages 5-7 and will not be repeated here. Applicants respectfully traverse this rejection.

As a threshold matter, a rejection under 35 U.S.C. § 103 must be supported using subject matter that was in the prior art under 35 U.S.C. § 102. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568 (Fed. Cir. 1987). Furthermore, Applicants believe that 35 U.S.C. § 103(c)(1) is relevant here and which states:

“[s]ubject matter developed by another person, which qualifies as prior art only under one or more of subsections (c), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.”

35 U.S.C. § 103(c)(1).

In view of the Office action’s admission on page 5 regarding Delcardayre’s deficient teachings, Applicants submit therefore that Delcardayre is not prior art under 35 U.S.C. § 103(a). Furthermore, Goldsmith is not prior art against the instant claims because under 35 U.S.C. § 103(c)(1), Goldsmith was owned by the same entity or subject to an obligation of assignment to the same entity as the instant application. The rejection of claims 52, 56, 58 and 60 under 35 U.S.C. § 103(a) based on Delcardayre and Goldsmith is thereby rendered moot.

Applicants submit that the claims are in compliance with 35 U.S.C. § 103 and respectfully request that the rejection be withdrawn.

4. Rejections of claims 1, 2, 4, 5, 7-9, 11, 15, 16, 18, 23, 26, 28, 30, 36, 39, 43, 44, 49, 54, 57, 59, 62, and 102 under 35 U.S.C § 112, first paragraph, enablement

The Office Action asserts a rejection of claims 1, 2, 4, 5, 7-9, 11, 15, 16, 18, 23, 26, 28, 30, 36, 39, 43, 44, 49, 54, 57, 59, 62, and 102 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

The Action specifically states that the specification, while being enabled for the claimed method using yeast or fungal cells as hosts, does not reasonably provide enablement for the other cell types such as mammalian, vertebrate, invertebrate, plant, and insect cells.

MPEP 2164.01 states that to satisfy the enablement requirement, an applicant must enable one of ordinary skill in the art to make and use the claimed invention. The standard for determining whether or not the specification meets the enablement requirement asks whether the "experimentation needed to practice the invention [is] undue or unreasonable." Enablement and whether any necessary experimentation is "undue" are analyzed with a view towards a weighing of the *Wands* factors, including (1) the quantity of experimentation required, (2) the amount of guidance presented, (3) the presence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the skill of those in the art, (7) the predictability of the art, and (8) the breadth of the claims. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988); MPEP 2164.01(a). However, enablement is not precluded by the necessity of even a considerable amount of experimentation in some cases, particularly if the experimentation is routine in nature, even when the art may be unpredictable. *U.S. v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988); *Ex Parte Mark*, 12 USPQ2d 1904(BPAI 1989); *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). Applicants respectfully submit that the specification provides ample support and teachings such that a person of ordinary skill in the art can make and use the claimed invention without undue experimentation.

The Action states that the breadth of the claim with regard to the initial cell population that comprises artificial chromosomes in the context of the claimed method is broad. It specifically alleges that the specification does not provide guidance for practicing the claimed method in host cells other than yeast or fungal cells.

Contrary to the position taken by the Office, the specification is more than adequate in its

disclosure of this information, such that the skilled artisan could practice the full scope of the invention as claimed. For example, the specification discloses that the two initial populations may be cells that can be mated to result in new diploid types. *See* paragraph [0109].

Contrary to the position taken by the Office, the specification is more than adequate in its disclosure of this information, such that the skilled artisan could practice the full scope of the invention as claimed. For example, the specification discloses that the two initial populations may be cells that can be mated or fused and that the resulting cell carries at least one artificial chromosome from each of the two populations that formed the resulting cells. *See* paragraphs [0035], [0109] and [0110]. The specification further discloses that other relevant species which can be mated or fused include prokaryotes [sic], and animal cells, including human cells (*See* paragraphs [0039] and [0040]), and that these cell should preferably be conditionally deficient in the abilities to undergo homologous recombination. *See* paragraph [0421]. It discloses furthermore, that in the case of heterologous genomic DNA, if eukaryotic donor organisms are used, it is preferable that the host cell has the ability to process the donor messenger RNA properly, *e.g.*, splice out introns. *Id.* The cells can be bacterial, archaeobacteria, or eukaryotic and can constitute a homogeneous cell line or mixed culture. *See* paragraph [422]. The specification discloses suitable mammalian cells to include those from, *e.g.*, mouse, rat, hamster, primate, and human. *Id.* It further discloses preferred prokaryotic host organisms, preferred eukaryotic host organisms, examples of insect cells, and examples of fungi. *See* paragraphs [0423]-[0428].

Regarding the use of artificial chromosomes, the specification discloses several types that may be used with the cells of the invention. In addition to use of yeast artificial chromosomes, it discloses that for eukaryotes the artificial chromosome may also be described as a nucleotide sequence of substantial length comprising a functional centromer [sic], functional telomeres, and at least one autonomous replicating sequence. It has the capacity to accommodate and express heterologous genes inserted therein. It is referred to as a mammalian artificial chromosome (MAC) when it contains an active mammalian centromere. *See* paragraph [0112]. The specification also discloses that plant artificial chromosome and insect artificial chromosome (BUGAC) refer to chromosomes that include plant and insect centromeres, respectively. *Id.* Finally, the specification discloses that a human artificial chromosome (HAC) refers to a chromosome that includes human

centromeres, and AVACs refer to avian artificial chromosomes. *Id.*, *See also*, paragraphs [0587]-[0589].

Therefore, Applicants argue that the disclosure provides ample guidance relative to the breadth of the claims, and such that one of skill in the art would understand that the full scope of the invention is reasonably enabled.

The Action also alleges that the state of the art at the time of filing does not provide teaching for how to accomplish the claimed method. The Action specifically alleges that whether the claimed method can be practiced with any cell type is unpredictable. As presented above, Applicants have detailed the sections of the specification that explicitly explain how to practice the invention using various cell types. Given the state of the art at the time of filing regarding use of artificial chromosomes and host cells, Applicants contend that one of skill in the art would understand, based on the disclosure of the specification, how to practice the claimed invention.

Applicants therefore have provided at least a reasonable amount of guidance to one of skill in the art regarding how he or she can proceed and direct further routine experimentation, in order to make and use the full scope of the invention. It follows from the teachings found within the specification and the knowledge of those skilled in the art that any further experimentation would merely be no more than routine in performing the method of mixing heterologous genes that covers the entire scope of the invention. Applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims under 35 U.S.C. § 112, first paragraph.

5. Rejections of claims 1, 2, 4, 5, 7-9, 11, 15, 16, 18, 23, 26, 28, 30, 36, 39, 43, 44, 49, 54, 57, 59, 62, and 102 under 35 U.S.C § 112, second paragraph

The Office Action asserts a rejection of claims 1, 2, 4, 5, 7-9, 11, 15, 16, 18, 23, 26, 28, 30, 36, 39, 43, 44, 49, 54, 57, 59, 62, and 102 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Applicants have amended claims 4, 8, 15, 16, 43, 62, and 80 to clarify claim scope. Applicants, however, respectfully traverse the rejection of claim 57 for reciting the term “substantially all.” Merriam-Webster’s Dictionary defines substantially as “being largely but not wholly that which is specified.” *See* Exhibit A. Applicants argue that one of skill in the art would understand the plain

meaning of “substantially all”, and therefore the term is not indefinite. Applicants also respectfully traverse the rejection of claim 54 as being indefinite for reciting the term “expression states.” Applicants direct the Examiner to paragraph [0453], which clearly states:

“By the term ‘Expression state’ is meant a state of gene expression (i.e the mRNA transcript population) in a specific cell, tissue, combination of tissues or organism or organisms of a given species as sampled at at any one time. Different expression states are found in different individuals, or in the same individual at different point in time, or in the same individual at different points its life-cycle or in the same individual under differing external conditions. The expression states of given cells or tissues of a given individual will also vary with respect to other cells or tissues of the same individual. Different expression states may also be obtained in the same organ or tissue in any one species or individual by exposing the tissues or organs to different environmental conditions comprising but not limited to changes in developmental stage, age, disease, infection, drought, humidity, salinity, exposure to xenobiotics, physiological effectors, temperature, pressure, pH, light, gaseous environment, chemicals such as toxins.”

The term is further defined in paragraphs [0454]-[0459]. Applicants argue that given the definition disclosed in the instant specification, one of skill in the art would understand the meaning of “expression states.” Applicants therefore contend that the term is not indefinite.

In view of the present amendment, Applicants respectfully submit that this rejection is moot. Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is in order and is respectfully requested.

6. Conclusion

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is therefore respectfully solicited.

If the Examiner believes it to be helpful in expediting the prosecution of this application, the Examiner is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
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Dated: March 15, 2010

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